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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/529,342	07/27/2000	DAVID J. CLARKE	39-206	8022

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EXAMINER	
YANG, NELSON C	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 07/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/529,342	CLARKE ET AL.	
	Examiner	Art Unit	
	Nelson Yang	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 April 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 2, 2005 has been entered.

2. Applicant's amendment of claim 42 is acknowledged and has been entered.

3. Claims 42-61 are currently pending.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 42-45, 51, 52, 54, 55, 58, 61, are rejected under 35 U.S.C. 103(a) as being unpatentable over Meers et al [US 6,339,069] in view of Parente et al [Parente et al, Mechanism of leakage of phospholipid vesicle contents induced by the peptide GALA, 1990, Biochemistry, 29, 8720-8728].

Meers et al teach a method comprising the steps of treating a sample with lipid vesicle particles incorporating a peptide that modulates the permeability of the particles in response to a predetermined metabolic signal from a targeted cell type (column 1, line 60 – column 2, line 20),

as discussed above in paragraphs 15-17. Meers et al further teach that the liposomes of this invention can incorporate a species activated on modulation of permeability (column 9, lines 25-48), comprising one or more "bioactive agents," which are compounds or compositions of matter having biological, including therapeutic or diagnostic, activity in animals (column 9, lines 25-48). Meers et al do not teach that the peptide is a cytolytic peptides such as GALA or KALA.

Parente et al, however, do teach the use of GALA (p.8720, col.1, lines 12-26), and further teaches that once GALA assembles to form a pore or channel (lysing the lipid vesicle), leakage is rapid and complete (p.8726, col. 2, lines 4-17). Since the amino acid sequence of GALA and N, Myristic GALA is essentially the same, with similar functions and pH sensitivities, GALA would be functionally equivalent to N, Myristic GALA and therefore it would be obvious to utilize GALA or N, Myristic GALA, in order permit rapid and complete leakage when GALA lyses the lipid vesicles.

Therefore it would be obvious to utilize a cytolytic peptide such as GALA or N, Myristic GALA in the method of Meers et al, in order to modulate the permeability of the particles in response to a predetermined metabolic signal from a targeted cell type, as taught by Parente et al, in order permit rapid and complete leakage.

6. With respect to claims 43-45, Parente et al teach that GALA is incorporated into the bilayer of the vesicles, and pores or channels are created within the bilayer membrane when peptide aggregate reaches a critical size (p.8721, col.2, lines 50-65).

7. With respect to claims 54 and 55, Meers et al teach that the species can be a dye or an enzyme (column 9, lines 25-48).

8. With respect to claims 58 and 61, Meers et al teach that the liposome can be used for diagnostic activity in animals (column 9, lines 25-29).

9. Claims 46-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meers et al [US 6,339,069 B1] in view of Parente et al [Parente et al, Mechanism of leakage of phospholipid vesicle contents induced by the peptide GALA, 1990, Biochemistry, 29, 8720-8728] and further in view of Li et al [US 5,512,294].

With respect to claims 46-49, Meers et al teach a method comprising the steps of treating a sample with lipid vesicle particles incorporating a cytolytic peptide that modulates the permeability of the particles in response to a predetermined metabolic signal from a targeted cell type (column 1, line 60 – column 2, line 20) and further incorporating a species activated on modulation of permeability (column 9, lines 25-48). Meers et al do not teach the use of antibodies as a binding agent for binding to an antigen on the cell type of interest.

Li et al do teach the use of a binding agent that is a antibody for binding to an antigen on the cell type of interest (column 2, lines 58-68). Li et al further teach that the use of binding agents allow for specific targeting and attachment to desired cell surface molecules (column 4, lines 43-48), in order to allow a variety of commercially available biotinylated antibodies to be used on the polymerized liposome particles (column 10, lines 1-3).

Therefore it would be obvious to use binding agents, as taught by Li et al, in the method of Meers et al in and Parente et al order to allow for specific targeting and attachment to desired cell surface molecules.

With respect to claim 50, Li et al teach liposomes where antibodies may be attached by the biotin-avidin biotinylated antibody sandwich (fig.16, column 9, lines 65-67).

10. Claims 55-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meers et al [US 6,339,069 B1] in view of Parente et al [Parente et al, Mechanism of leakage of phospholipid vesicle contents induced by the peptide GALA, 1990, Biochemistry, 29, 8720-8728] and further in view of Levinson et al [US 6,020,142].

With respect to claims 56-57, Meers et al teach a method comprising the steps of treating a sample with lipid vesicle particles incorporating a cytolytic peptide that modulates the permeability of the particles in response to a predetermined metabolic signal from a targeted cell type (column 1, line 60 – column 2, line 20) and further incorporating a species activated on modulation of permeability (column 9, lines 25-48). Meers et al teach that the species can be a dye or an enzyme (column 9, lines 25-48). Meers et al do not teach that the species is a substrate for an enzyme or is glucose oxidase.

Levinson et al, however, teach the use of a delivery complex such as liposomes (column 3, lines 5-12) for delivering enzymes and substrates such as glucose oxidase (column 25, lines 40-42) in order to label RATH gene peptide-specific antibodies. This is important as the RATH1.1 gene product has been demonstrated to act as a mediator of signal transduction events, and and the detection of compounds which modulate the RATH gene product would allow for the diagnostic evaluation, prognosis, and treatment of immune disorders involving T cell activation (column 1, lines 29-62).

Therefore one of ordinary skill in the art would have been motivated to have the liposomes deliver enzymes and substrates such as glucose oxidase, as suggested by Levinson et al, in the method of Meers et al and Parente et al, to in order to study specific cells such as T

cells, such that the diagnostic evaluation, prognosis, and treatment of immune disorders involving T cell activation is possible.

11. Claim 59 is rejected under 35 U.S.C. 103(a) as being unpatentable over Meers et al [US 6,339,069 B1] in view of Parente et al [Parente et al, Mechanism of leakage of phospholipid vesicle contents induced by the peptide GALA, 1990, Biochemistry, 29, 8720-8728] and further in view of Robinson et al [US 5,994,149].

Meers et al teach a method comprising the steps of treating a sample with lipid vesicle particles incorporating a cytolytic peptide that modulates the permeability of the particles in response to a predetermined metabolic signal from a targeted cell type (column 1, line 60 – column 2, line 20) and further incorporating a species activated on modulation of permeability (column 9, lines 25-48). Meers et al further teach that the liposome can be used for diagnostic activity in animals (column 9, lines 25-29). Meers et al do not teach the detection of pathogenic cells in foodstuffs.

Robinson et al, however, do teach the analysis of foodstuffs for pathogenic cells using liposomes (column 4, lines 19-24). Robinson et al further teach that it would be desirable to have a test kit that would eliminate operator error, and have a predictably accurate and reproducible rate of identification of pathogenic fungi, yeasts and molds (column 1, lines 16-45).

Therefore it would be obvious to teach the detection of pathogenic cells in foodstuffs, as taught by Robinson et al, in the method of Meers et al and Parente et al, in order to have a test kit that would eliminate operator error, and have a predictably accurate and reproducible rate of identification of pathogenic fungi, yeasts and molds.

12. Claim 60 is rejected under 35 U.S.C. 103(a) as being unpatentable over Meers et al [US 6,339,069 B1] in view of Parente et al [Parente et al, Mechanism of leakage of phospholipid vesicle contents induced by the peptide GALA, 1990, Biochemistry, 29, 8720-8728] and further in view of Blondin et al [US 4,808,517].

Meers et al teach a method comprising the steps of treating a sample with lipid vesicle particles incorporating a cytolytic peptide that modulates the permeability of the particles in response to a predetermined metabolic signal from a targeted cell type (column 1, line 60 – column 2, line 20) and further incorporating a species activated on modulation of permeability (column 9, lines 25-48). Meers et al further teach that the liposome can be used for diagnostic activity in animals (column 9, lines 25-29). Meers et al do not teach the detection of pathogenic cells in foodstuffs. Meerss et al do not teach the detection of pathogenic cells in water samples.

Blondin et al, however, do teach a method of using of lipid vesicles (column 4, lines 9-24) for the detection of toxins in water samples (column 8, lines 20-32) that is economical and efficient and can be quickly and easily performed (column 2, lines 64-68).

Therefore it would be obvious to use the method of Meers et al and Parente et al to analyze water samples for pathogens as taught by Blondin et al, in order to detect toxins economically, efficiently, quickly and easily.

13. Claims 42, 53-55, 58, 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meers et al [US 6,339,069 B1] in view of Rizzo et al [Rizzo et al, *Alamethicin incorporation in lipid bilayers: a thermodynamic study*, 1987, Biochemistry, 26, 2751-2759].

Meers et al teach a method comprising the steps of treating a sample with lipid vesicle particles incorporating a peptide that modulates the permeability of the particles in response to a

predetermined metabolic signal from a targeted cell type (column 1, line 60 – column 2, line 20), as discussed above in paragraphs 15-17. Meers et al further teach that the liposomes of this invention can incorporate a species activated on modulation of permeability (column 9, lines 25-48), comprising one or more "bioactive agents," which are compounds or compositions of matter having biological, including therapeutic or diagnostic, activity in animals (column 9, lines 25-48). Meers et al do not teach that the peptide is a cytolytic peptides such as alamethicin.

Rizzo et al, however, do teach the use of alamethicin with phospholipid vesicles as conducting pores (p.2751, col. 1-2, p.2758, col. 1, lines 1-6). Rizzo et al further suggest the use of alamethicin as a "molecular switch" by means of aggregation in the membrane (p.2758, col. 1, lines 27-33), and that very high ratios of peptide to lipid can be reached without apparent saturation (p.2756, col.1, lines 38-45).

Therefore it would be obvious to use alamethicin with lipid vesicle particles, as taught by Rizzo et al, in the method of Meers et al, in order to introduce "a molecular switch" by means of aggregation in the membrane, and to achieve very high ratios of peptide to lipid without apparent saturation.

14. With respect to claims 43-45, alamethicin is incorporated into the lipid bilayer membrane (p.2756, col.1, lines 35-45).

15. With respect to claims 54 and 55, Meers et al teach that the species can be a dye or an enzyme (column 9, lines 25-48).

16. With respect to claims 58 and 61, Meers et al teach that the liposome can be used for diagnostic activity in animals (column 9, lines 25-29).

17. Claims 46-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meers et al [US 6,339,069 B1] in view of Rizzo et al [Rizzo et al, *Alamethicin incorporation in lipid bilayers: a thermodynamic study*, 1987, Biochemistry, 26, 2751-2759] and further in view of Li et al [US 5,512,294].

With respect to claims 46-49, Meers et al teach a method comprising the steps of treating a sample with lipid vesicle particles incorporating a cytolytic peptide that modulates the permeability of the particles in response to a predetermined metabolic signal from a targeted cell type (column 1, line 60 – column 2, line 20) and further incorporating a species activated on modulation of permeability (column 9, lines 25-48). Meers et al do not teach the use of antibodies as a binding agent for binding to an antigen on the cell type of interest.

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Therefore it would be obvious to use binding agents, as taught by Li et al, in the method of Meers et al in and Rizzo et al order to allow for specific targeting and attachment to desired cell surface molecules.

18. With respect to claim 50, Li et al teach liposomes where antibodies may be attached by the biotin-avidin biotinylated antibody sandwich (fig.16, column 9, lines 65-67).

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bilayers: a thermodynamic study, 1987, Biochemistry, 26, 2751-2759] and further in view of Levinson et al [US 6,020,142].

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21. Claim 60 is rejected under 35 U.S.C. 103(a) as being unpatentable over Meers et al [US 6,339,069 B1] in view of Rizzo et al [Rizzo et al, *Alamethicin incorporation in lipid bilayers: a*

thermodynamic study, 1987, Biochemistry, 26, 2751-2759] and further in view of Blondin et al [US 4,808,517].

Meers et al teach a method comprising the steps of treating a sample with lipid vesicle particles incorporating a cytolytic peptide that modulates the permeability of the particles in response to a predetermined metabolic signal from a targeted cell type (column 1, line 60 – column 2, line 20) and further incorporating a species activated on modulation of permeability (column 9, lines 25-48). Meers et al further teach that the liposome can be used for diagnostic activity in animals (column 9, lines 25-29). Meers et al do not teach the detection of pathogenic cells in foodstuffs. Meerss et al do not teach the detection of pathogenic cells in water samples.

Blondin et al, however, do teach a method of using of lipid vesicles (column 4, lines 9-24) for the detection of toxins in water samples (column 8, lines 20-32) that is economical and efficient and can be quickly and easily performed (column 2, lines 64-68).

Therefore it would be obvious to use the method of Meers et al and Rizzo et al to analyze water samples for pathogens as taught by Blondin et al, in order to detect toxins economically, efficiently, quickly and easily.

Response to Arguments

22. Applicant's arguments with respect to claims 42-61 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

23. No claims are allowed.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571) 272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571)272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

25. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Nelson Yang
Patent Examiner
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Christopher L. Chin

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7/8/05